Pathophysiology of Diabetes

Diabetes is a chronic metabolic disorder in which the body cannot metabolize carbohydrates, fats, and proteins because of a lack of, or ineffective use of, the hormone insulin. Diabetes is classified into three primary types that are different disease entities but share the symptoms and complications of hyperglycemia (high blood glucose).

Impaired glucose tolerance, formerly known as "borderline diabetes" is a degree of hyperglycemia that may precede type 2 diabetes.

I. Type 1 (previously called insulin dependent diabetes mellitus (IDDM) or juvenile-onset diabetes)

A. Causes

1. Genetic predisposition.
2. Environmental exposure: virus, toxin, stress.
3. Autoimmune reaction: beta-cells that produce insulin in the pancreas are destroyed. When 80-90% of the beta-cells are destroyed, overt symptoms occur.

B. Characteristics

1. Usually occurs before 30 years of age, but can occur at any age. Peak incidence occurs during puberty, around 10-12 years of age in girls and 12-14 years in boys.*
2. Abrupt onset of signs and symptoms of hyperglycemia: increased thirst and hunger, frequent urination, weight loss, and fatigue.
3. Ketosis prone.

C. Treatment

1. Insulin by injection with syringes or pumps
2. Diet
3. Exercise
4. Education
5. Monitoring

II. Type 2 (previously called non-insulin-dependent diabetes mellitus, NIDDM, or adult-onset diabetes)

A. Causes

1. Insulin resistance: unable to utilize insulin that the body makes because of cell-receptor defect; glucose is unable to be absorbed into cells for fuel.
2. Decreased insulin secretion: pancreas does not secrete enough insulin in response to glucose levels.
3. Excess production of glucose from the liver: result of defective insulin secretory response; dawn phenomenon (see glossary) is an example.

B. Characteristics

1. Usually occurs after 30 years of age, but is now occurring in children and adolescents.
2. Increased prevalence in some ethnic groups, e.g., African Americans, Hispanic/Latino, Native Americans, Asian Americans, and Pacific Islanders.
3. Strong genetic predisposition.
4. Frequently obese.
5. Not prone to ketoacidosis until late in course or with prolonged hyperglycemia.
6. May or may not have symptoms of hyperglycemia.
7. May also have extreme tiredness, blurred vision, delayed healing, numbness and tingling of hands and feet, recurring yeast infection.
8. Children between the ages of 10-19 that have one or more of the following are at an increased risk:
   - Family history
   - Member of certain ethnic populations listed above in B.2.
   - Overweight
   - Sedentary lifestyle

* Source: American Diabetes Association. Diabetes Facts. November, 2003.

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- Pre-puberty.
- Signs of insulin resistance or conditions associated with insulin resistance (acanthosis nigricans [dirty-neck syndrome], hypertension [high blood pressure], dyslipidemia [lipoproteins inbalance], polycystic ovarian syndrome [PCOS]).

C. Treatment

1. Diet/weight management
2. Exercise/increase physical activity
3. Oral hypoglycemic/antihyperglycemic agents, insulin sensitizers, or insulin
4. Education
5. Monitoring
6. Treatment of comorbid conditions (e.g., hypertension, lipid abnormalities)

III. Gestational Diabetes Mellitus (GDM)

A. Causes

1. Insulin resistance due to pregnancy
2. Genetic predisposition

B. Characteristics

1. Carbohydrate intolerance during pregnancy identified via 1-hour screen using a 50-g oral glucose load (performed between 24th and 28th week of gestation unless otherwise indicated). If the 1-hour screen for glucose is ≥140 mg/dl (≥7.8 mmol/l), a full diagnostic 100-g, 3-hour oral glucose tolerance test (OGTT) is indicated.

C. Treatment

1. Diet: provide adequate calories without hyperglycemia or ketonemia
2. Exercise: program that does not cause fetal distress, contractions, or hypertension (>140/90 mmHg).
3. Insulin: if unable to consistently maintain blood glucose ≤95 mg/dl fasting (≤5.3 mmol/l) and ≤140 mg/dl (≤7.8 mmol/l) 1 hour postprandial and ≤120 mg/dl (≤6.7 mmol/l) 2 hours postprandial.

D. Monitoring

1. Blood glucose: required to determine effectiveness of treatment and possible need for insulin. Glucose should be checked fasting and 1-2 hours postprandial.
2. Ketones: test for ketones using first morning urine sample. Presence of ketones may indicate starvation rather than hyperglycemic ketosis.

For more information about the pathophysiology of diabetes, see the American Diabetes Association's 2004 position statement "Diagnosis and Classification of Diabetes Mellitus" *Diabetes Care*, Volume 27, Supplement 1, pages S5-S10.

For more information about the dyslipidemia often associated with diabetes, please see the American Diabetes Association's 2003 consensus statement, "The Management of Dyslipidemia in Children and Adolescents with Diabetes", *Diabetes Care*, Volume 26, number 7, pages 2194-2197.

Both of the above-mentioned articles can be accessed at: http://care.diabetesjournals.org/.

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